REMARKS

Claims 61-115 are pending. Claims 67, 69, 70, 74, 76, 78, 80, 81, 83, 85, 87, 95-97, 101, 103, 105, 107, 108, 110, 112, and 114 are under examination. Claims 67 and 95 have been amended. Support for the amendments can be found throughout the specification and the claims as filed. In particular, support for the amendment to claims 67 and 95 can be found, for example, on page 39, lines 21-28, and Example VII, page 66, lines 17-27. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested. Entry of the proposed amendments is respectfully submitted to be proper because the amendments are believed to place the claims in condition for allowance.

The rejection of claims 67, 69, 83, 85, 95, 96, 110 and 112 under 35 U.S.C. § 103 as allegedly obvious over Blanchard et al., WO 02/30430, in view of Sung et al., U.S. Patent No. 6,624,138, and in further view of ElGenidi, Eur. J. Cancer 37:S357 (2001), is respectfully traversed. Applicants respectfully maintain, for the reasons of record, that the claimed methods are unobvious over Blanchard et al., alone or in combination with Sung et al. and/or ElGenidi.

Applicants respectfully maintain that none of Blanchard et al., alone or in combination with Sung et al. and/or ElGenidi, teaches or suggests Applicants' claimed methods. Nevertheless, to further prosecution and without prejudice to Applicants pursuing the previous claims in a related application, claims 67 and 95 have been amended to recite the synergistic activity of the combination of paricalcitol and an anti-cancer agent in reducing cell proliferation. Claim 67, as amended, is directed to a method of reducing the severity of a proliferative disorder by administering to an individual having the proliferative disorder, wherein the proliferative disorder is selected from myelodysplastic syndrome, leukemia, acute myelocytic leukemia, acute lymphocytic leukemia, multiple myeloma, breast cancer, colon cancer and prostate cancer, an effective amount of paricalcitol and an anti-cancer agent, wherein the combination of paricalcitol and the anti-cancer agent synergistically reduces cell proliferation. Claim 95 is directed to a method of reducing cancer recurrence, comprising administering to an individual in cancer remission, wherein the cancer in remission is selected from myelodysplastic syndrome, leukemia, acute myelocytic leukemia, acute lymphocytic leukemia, multiple myeloma, breast cancer, colon cancer and prostate cancer, an effective amount of paricalcitol and an anti-cancer

agent, wherein the combination of paricalcitol and the anti-cancer agent synergistically reduces cancer cell proliferation.

Applicants respectfully maintain, for the reasons of record, that Blanchard et al. does not teach or suggest the claimed methods of reducing the severity of a proliferative disorder. At best, Blanchard et al. describes the use of vitamin D_2 compounds for reducing, preventing or treating hair loss (alopecia) induced by a chemotherapeutic agent. However, Blanchard et al. provides no teaching or suggestion of the claimed methods of reducing the severity of a proliferative disorder or reducing cancer recurrence. Furthermore, as discussed in the previous response, ElGenidi merely corroborates that alopecia is a side effect of chemotherapy, and in fact describes the use of a digital scalp cooling system for the prevention of chemotherapy-induced alopecia. Moreover, Sung et al. describes solidifiable drug-containing biological material and a huge laundry list of numerous exemplary drugs suitable for inclusion in the material, including analgesics, antibiotics, antidepressants, etc. However, Sung et al. provides no teaching or suggestion of using paricalcitol to reduce the severity of a proliferative disorder or reduce cancer recurrence, as in the claimed methods.

Moreover, none of Blanchard et al., Sung et al. and/or ElGenidi, alone or in combination, teaches or suggests the claimed methods of reducing a proliferative disorder or cancer recurrence by administering paricalcitol and an anti-cancer agent, wherein the combination of paricalcitol and the anti-cancer agent synergistically reduces cell proliferation. Based on the description in Blanchard et al., Sung et al. and/or ElGenidi, one skilled in the art would have had no reasonable expectation of success of achieving the claimed methods, in which the combination of paricalcitol and an anti-cancer agent synergistically reduces cell proliferation.

To establish a *prima facie* case, the Office must satisfy three requirements. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, should contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. See *Karsten Mfg. Corp. v. Cleveland Gulf Co.*, 242 F.3d 1376, 1385, 58 U.S.P.Q.2d 1286, 1293 (Fed. Cir. 2001); *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1352, 48 U.S.P.Q.2d 1225, 1232 (Fed. Cir. 1998); *Northern Telecom v. Datapoint Corp.*, 908 F.2d 931, 934, 15 U.S.P.Q.2d 1321, 1323 (Fed. Cir. 1990).

Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. In other words, a hindsight analysis is not allowed. See *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991); *In re Erlich*, 3 U.S.P.Q.2d 1011, 1016 (Bd. Pat. App. & Int. 1986). Lastly, the prior art reference or combination of references must teach or suggest all the limitations of the claims. See *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

Applicants respectfully maintain that the Office has not met the burden the law allocates to it with regard to establishing a *prima facie* case of obviousness, which requires that the prior art references relied upon give rise to the requisite motivation to combine their content and, when viewed in combination, provide the skilled person with a reasonable expectation of success to achieve the claimed invention, and further teach or suggest all the limitations of the claims. Applicants respectfully maintain that a *prima facie* case of obviousness has not been established, and therefore the claimed methods are unobvious over Blanchard et al., alone or in combination with Sung et al. and/or ElGenidi. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 67, 69, 70, 76, 80, 81, 87, 95-97, 103, 107, 108 and 114 under 35 U.S.C. § 103 as allegedly obvious over Blanchard et al., *supra*, in view of Tidmarsh et al., U.S. Patent No. 7,001,888, and in further view of Sung et al., *supra*, and in further view of ElGenidi, *supra*, is respectfully traversed. Applicants respectfully maintain, for the reasons of record, that the claimed methods are unobvious over Blanchard et al., alone or in combination with Tidmarsh et al. and/or Sung et al. and/or ElGenidi.

As discussed above and in the previous response, none of Blanchard et al. and/or Sung et al. and/or ElGenidi teaches or suggests Applicants' claimed methods. Moreover, Applicants respectfully submit that Tidmarsh et al. does not cure the deficiencies of Blanchard et al. and/or Sung et al. and/or ElGenidi. At best, Tidmarsh et al. describes compounds for treating cancer. However, Applicants respectfully maintain that the claimed methods of reducing the severity of a proliferative disorder and reducing cancer recurrence are neither taught nor suggested in any of Blanchard et al., Sung et al., ElGenidi or Tidmarsh et al., alone or in combination. Furthermore,

none of these references, alone or in combination, teaches or suggest the claimed methods of reducing a proliferative disorder or cancer recurrence by administering paricalcitol and an anti-cancer agent, wherein the combination of paricalcitol and the anti-cancer agent synergistically reduces cell proliferation. For the reasons of record and as discussed above, Applicants respectfully maintain that a *prima facie* case of obviousness has not been established, and therefore the claimed methods are unobvious over Blanchard et al., alone or in combination with Sung et al. and/or ElGenidi and/or Tidmarsh et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 67, 69, 74, 78, 95, 96, 101 and 105 under 35 U.S.C. § 103 as allegedly obvious over Blanchard et al., *supra*, in view of Shashoua et al., U.S. Patent No. 5,795,909, and in further view of Sung et al., *supra*, and in further view of ElGenidi, *supra*, is respectfully traversed. Applicants respectfully maintain, for the reasons of record, that the claimed methods are unobvious over Blanchard et al., alone or in combination with Shashoua et al. and/or Sung et al. and/or ElGenidi.

As discussed above and in the previous response, none of Blanchard et al. and/or Sung et al. and/or ElGenidi teaches or suggests Applicants' claimed methods. Moreover, Applicants respectfully submit that Shashoua et al. does not cure the deficiencies of Blanchard et al. and/or Sung et al. and/or ElGenidi. At best, Shashoua et al. describes conjugates of cis-docosohexaenoic acid and taxanes for treating proliferative disorders. However, Applicants respectfully maintain that the claimed methods of reducing the severity of a proliferative disorder and reducing cancer recurrence are neither taught nor suggested in any of Blanchard et al., Sung et al., ElGenidi or Shashoua et al., alone or in combination. Furthermore, none of these references, alone or in combination, teaches or suggest the claimed methods of reducing a proliferative disorder or cancer recurrence by administering paricalcitol and an anti-cancer agent, wherein the combination of paricalcitol and the anti-cancer agent synergistically reduces cell proliferation. For the reasons of record and as discussed above, Applicants respectfully submit that a *prima facie* case of obviousness has not been established, and therefore the claimed methods are unobvious over Blanchard et al., alone or in combination with Sung et al. and/or ElGenidi and/or Shishoua et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP

/Deborah L. Cadena/

Deborah L. Cadena
Registration No. 44,048

4370 La Jolla Village Drive, Suite 700
San Diego, CA 92122
Phone: 858.535.9001 DLC:llf
Facsimile: 858.597.1585
Date: March 20, 2008

Please recognize our Customer No. 41552 as our correspondence address.